## REMARKS

Applicants have studied the Office Action mailed April 24, 2006 and have made amendments to the specification. It is respectfully submitted that the application, as amended, is in condition for allowance. Reconsideration and allowance of the pending claims in view of the above amendments and following remarks is respectfully requested.

**Sequence Compliance/Drawings:**

The Examiner stated that this application fails to comply with the requirements of 37 CFR 1.821-1.825.

Applicants hereby submit Replacement Sheets of Figures, which add sequence identifiers for sequences in Figures 2A, 2C, 2D, and 3O-3Y that must be identified by such, along with a Substitute Sequence Listing that includes SEQ ID NOS:7-61 which correspond to the polynucleotide sequences presented in Figures 3O-3Y.

**Priority:**

Applicants respectfully assert that, because the priority information was provided in an Application Data Sheet (filed with the application as originally submitted on August 20, 2003), the priority information does not also need to be in the first sentence of the specification. Furthermore, the filing receipt mailed November 18, 2003 provides verification of the priority information for the present application and also indicates the patent number for the issued priority application.

**Title:**

The Examiner stated that the title of the invention is not descriptive, and a new title is required that is clearly indicative of the invention to which the claims are directed.

The title is hereby amended to be more clearly indicative of the invention to which the claims are directed, as indicated above by the amendments to the specification.

**Objection to the specification (description of figures):**

The Examiner objected to the specification for failing to provide a brief description of each individual Figure.

In response, the "Description of the Figure Sheets" section of the specification is hereby amended, as indicated above by the amendments to the specification, for consistency with the page numbering of the Figures.

**Rejection of claims 18-21 under 35 USC §112, 2nd paragraph:**

The Examiner rejected claims 18-21 under 35 USC §112, 2nd paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention because there is insufficient antecedent basis for the limitation of "the antibody" because independent claims 3 and 15 recite "an isolated antibody" not a conjugated/coupled antibody.

Claims 18 and 20 are hereby amended for clarity. Antibodies coupled to a detectable substance are described at, for example, the second full paragraph on page 24 of the specification.

**Objection to the specification (antecedent basis):**

The Examiner objected to the specification as failing to provide proper antecedent basis for the claimed subject matter, and Applicant is required to identify the written support for claims 22-25, particularly the claimed limitation of "pharmaceutically acceptable carrier".

In response, Applicants respectfully assert that the phrase "pharmaceutically acceptable carrier" does have written support in the specification as originally filed. In particular, claim 10 as originally filed recites "A pharmaceutical composition comprising an agent identified by the method of claim 9 and a pharmaceutically acceptable carrier therefor". The "agent" recited in this claim can be an antibody.

**Rejection of claims 15, 17, 19, 21, 23, and 27 under 35 USC §112, 1st paragraph:**

The Examiner rejected claims 15, 17, 19, 21, 23, and 27 under 35 USC §112, 1st paragraph, as failing to comply with the enablement requirement because these claims recite "polypeptide comprises SEQ ID NO:2, and the specification discloses only protein with amino acid sequence of SEQ ID NO:2, however, the term "comprise" in the claims are open-ended and expands the sequence of SEQ ID NO:2 to include additional non-disclosed amino acid residues

outside of the sequence shown in SEQ ID NO:2. The Examiner also states that neither does the specification provide a sufficient enabling description of an antibody reactive towards a genus of a "polypeptide comprises SEQ ID NO:2".

To expedite prosecution, claims 15, 17, 19, 21, 23, and 27 are hereby canceled.

**Rejection of claims 3 and 15-17 under 35 USC §102(b):**

The Examiner rejected claims 3 and 15-17 under 35 USC §102(b) as being anticipated by Robinson (U.S. Patent 5,589,372) as evidenced by Bost et al. (*Immunol. Invest.* 1988; 17:577-586) and Bendayan (*J. Histochem. Cytochem.* 1995; 43:881-886).

In making this rejection, the Examiner states that Robinson teaches isolated polypeptide of squalene synthetase comprising an amino acid sequence eof SEQ ID NO:6 that shares 98.4% homology of polypeptide with amino sequence of SEQ ID NO:2 of the instant claims, and Robinson further teaches that antibodies capable of binding squalene synthetase with amino acid of SEQ ID NO:6 such as monoclonal antibody can be made. The Examiner states that, as evidenced by Bost et al., antibodies can be specific and cross-react with the antigen, and, as further evidenced by Bendayan, the specific reactivity of a monoclonal antibody can be highly specific yet cross-react with antigens from different species or even distinct proteins not related to the original antigen. The Examiner asserts that, given the high degree of sequence homology between the prior art squalene synthetase of SEQ ID NO:6 and instant polypeptide comprising SEQ ID NO:2, monoclonal antibody that binds to the prior art synthetase would bind shared regions of sequence identity of the instant polypeptide comprising SEQ ID NO:2.

In response, Applicants respectfully assert that Robinson does not anticipate claims 3 and 15-17.

The Examiner asserts that an antibody taught by Robinson will inherently cross-react and thus bind to the same polypeptides (i.e., polypeptides consisting of SEQ ID NO:2) as the instantly claimed antibodies, thereby anticipating the instant claims. However, inherency may only be relied upon where the consequences of following the reference disclosure always necessarily results in the claimed invention. If there is not a reasonable certainty that the claimed subject matter will necessarily result, the rejection is not proper.

Specifically, in order for an antibody as taught by Robinson to inherently anticipate the instant claims, the antibody as taught by Robinson must necessarily selectively bind to the

polypeptides recited in the instant claims (i.e., polypeptides consisting of SEQ ID NO:2). It is not sufficient that the antibody as taught by Robinson may possibly or probably bind to the polypeptides recited in the instant claims.

However, this "possibly or probably" standard appears to be the standard that the Patent Office is relying on for the rejection of claims 3 and 15-17 under 35 USC §102(b). The Examiner has cited a reference that teaches an antibody that may possibly or probably selectively bind to polypeptides of SEQ ID NO:2 because the reference teaches that antibodies can be made to a protein (SEQ ID NO:6 of Robinson) that shares 98.4% homology with SEQ ID NO:2 of the instant claims. However, this does not mean that the reference antibody must necessarily selectively bind to polypeptides of SEQ ID NO:2.

It is Applicant's position that an antibody as taught by Robinson does not necessarily selectively bind to polypeptides of SEQ ID NO:2 because different epitopes must necessarily exist in the polypeptide of SEQ ID NO:2 of the instant application compared with SEQ ID NO:6 of Robinson because of the differences that exist in their amino acid sequences. For example, the amino acid sequence of instant SEQ ID NO:2 differs by at least 1.6% from SEQ ID NO:6 of Robinson. Any antibody-binding epitopes that span any amino acid residues that are included in this 1.6% portion that differs between instant SEQ ID NO:2 and SEQ ID NO:6 of Robinson will serve to differentiate instant SEQ ID NO:2 from SEQ ID NO:6 of Robinson with respect to antibody recognition and specificity. Therefore, due to these differences in the protein structures, an antibody as taught by Robinson clearly does not necessarily cross-react with the same proteins as the antibodies of claims 3 and 15-17.

Accordingly, Applicants respectfully request that the rejection of claims 3 and 15-17 under 35 USC §102(b) be reconsidered and withdrawn.

**Rejection of claims 3, 15-25, and 26-27, under 35 USC §103(a):**

The Examiner rejected claims 3 and 15-25 under 35 USC §103(a) as being unpatentable over Robinson in view of Bost et al., Bendayan, and Harlow et al. The Examiner also rejected claims 26-27 under 35 USC §103(a) as being unpatentable over Pluckthun et al. in view of Robinson, Bost et al., and Bendayan.

In making this rejection against claims 3 and 15-25, the Examiner states that Robinson, Bost et al., and Bendayan do not teach an antibody coupled to a detectable substance and a

pharmaceutically acceptable carrier, however Harlow et al. teach methods of immunoassay using antibodies coupled directly to a detectable substance and also teach examples of coupling antibodies to detectable substance buffers such as PBS, a well known pharmaceutically acceptable carrier. In making this rejection against claims 26-27, the Examiner states that Pluckthun et al. teach that recombinant fragments such as Fab, $F(ab')_2$, and Fv provide improved performance *in vivo* and in a variety of *in vitro* assays. The Examiner states that, given the teachings of Pluckthun et al. regarding antibody fragments and the teachings of Robinson, Bost et al., and Bendayan providing method and use of antibodies that bind polypeptide of SEQ ID NO:2, the ordinary artisan would have been motivated to make antibody fragments that bind to the polypeptide of SEQ ID NO:2 and would have had a reasonable expectation of success.

However, in light of the discussion above in regards to the anticipation rejection under 35 USC §102(b) in view of Robinson as evidenced by Bost et al. and Bendayan, it is clear that neither Harlow et al. nor Pluckthun et al., even in combination with any of Robinson, Bost et al., and Bendayan, makes obvious any of claims 3, 15-25, and 26-27 due at least to the different antibody-binding epitopes that necessarily exist because of the amino acid sequence differences in SEQ ID NO:6 of Robinson compared with SEQ ID NO:2 of the instant application (for example, SEQ ID NO:2 differs from SEQ ID NO:6 of Robinson by at least 1.6%). This obviates the teachings of Harlow et al. and Pluckthun et al. with respect to Robinson, Bost et al., and Bendayan as applied to claims 3, 15-25, and 26-27 under 35 USC §103(a).

Accordingly, Applicants respectfully request that the rejections of claims 3, 15-25, and 26-27 under 35 USC §103(a) be reconsidered and withdrawn.

## Conclusions

Claims 1-2, 15, 17, 19, 21, 23, and 27-29 are hereby canceled, and claims 18 and 20 are hereby amended. As such, claims 3, 16, 18, 20, 22, and 24-26 are pending and under consideration. Claims 1-2 and 28-29 were withdrawn from consideration by the Examiner as being directed to non-elected inventions, and are hereby canceled for this reason.

In view of the above amendments and remarks, Applicants respectfully submit that the application and claims are in condition for allowance, and request that the Examiner reconsider and withdraw the objections and rejections. If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is invited to call the undersigned agent at (240) 453-3812 should the Examiner believe a telephone interview would advance prosecution of the application.

Respectfully submitted,
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